



VOLUME 3 – ISSUE 10: TRANSCRIPT

Featured Cases: HCV Screening and Natural History

Our guest author is David Thomas, MD, Professor of Medicine and Director of the Division of Infectious Diseases at the Johns Hopkins University School of Medicine in Baltimore.

After participating in this activity, the participant will demonstrate the ability to:

- Discuss why patients with no risk factor except being born between 1945 and 1965 should be tested for HCV.
■ Describe current noninvasive testing that can be used to detect cirrhosis.
■ Explain why HCV RNA should be used to detect acute HCV infection.

This discussion, offered as a downloadable audio file and companion transcript, covers the topic of HCV screening and natural history, as well as case-study scenarios for the clinical practice. This program is a follow up to the Volume 3, Issue 9 eViralHepatitis Review newsletter—HCV Screening and Natural History.

Unlabeled/Unapproved Uses

Dr. Thomas has indicated that in today's discussion he will not reference the unlabeled or unapproved uses of any drugs or products.

MEET THE AUTHOR



David Thomas, MD

Professor of Medicine
Director of the Division of Infectious Diseases
The Johns Hopkins University School of Medicine
Baltimore, Maryland

Faculty Disclosure

Dr. Thomas has disclosed that he has received grants from Gilead Sciences, Inc. and Merck.

Release Date
May 27, 2014

Expiration Date
May 26, 2016

PROGRAM DIRECTORS

Mark S. Sulkowski, MD
Professor of Medicine
Medical Director, Viral Hepatitis Center
Divisions of Infectious Diseases and Gastroenterology/Hepatology
The Johns Hopkins University School of Medicine
Baltimore, Maryland

Raymond T. Chung, MD
Associate Professor of Medicine
Director of Hepatology, Harvard Medical School
Vice Chief of Gastroenterology
Massachusetts General Hospital
Boston, Massachusetts

Julie McArthur, MS, CRNP
Adult Nurse Practitioner
Division of Infectious Disease
The Johns Hopkins University School of Medicine
Baltimore, Maryland

ACCREDITATION STATEMENTS**Physicians**

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing. The Johns Hopkins University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Nurses

The Institute for Johns Hopkins Nursing is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

The Institute for Johns Hopkins Nursing and the American Nurses Credentialing Center do not endorse the use of any commercial products discussed or displayed in conjunction with this educational activity.

CREDIT DESIGNATIONS**Physicians**

eNewsletter: The Johns Hopkins University School of Medicine designates this enduring material for a maximum of 1.0 *AMA PRA Category 1 Credit(s)*[™]. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Podcast: The Johns Hopkins University School of Medicine designates this enduring material for a maximum of 0.5 *AMA PRA Category 1 Credit(s)*[™]. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Nurses

eNewsletter: This 1 contact hour Educational Activity is provided by The Institute for Johns Hopkins Nursing. Each newsletter carries a maximum of 1 contact hour or a total of 6 hours for the six newsletters in this program.

Podcast: This 0.5 contact hour Educational Activity is provided by the Institute for Johns Hopkins Nursing. Each podcast carries a maximum of 0.5 contact hours a total of 3 contact hours for the six podcasts in this program.

SUCCESSFUL COMPLETION

To take the post-test for eViralHepatitis Review you will need to visit the [Johns Hopkins University School of Medicine's CME website](#) and the [Institute for Johns Hopkins Nursing's website](#). If you have already registered for other Hopkins CE programs at these sites, simply enter the requested information when prompted. Otherwise, complete the registration form to begin the testing process. A passing grade of 70% or higher on the post-test/evaluation is required to receive CE credit.

NOTE: If you have already registered for other Hopkins CME programs on their prospective websites simply enter the requested information when prompted.

There are no fees or prerequisites for this activity.

This activity is supported by educational grants from AbbVie, Inc., Boehringer Ingelheim Pharmaceuticals, Inc., and Genentech, Inc.

LAUNCH DATE

August 27, 2013; activities expire 2 years from the date of publication.

INTENDED AUDIENCE

The target audience (clinicians) for the HBV curriculum includes:

- Primary: primary care physicians (PCPs), OB/GYNs, physician assistants (PAs), nurse practitioners (NPs), community gastroenterologists and others who care for patients of Asian and West African descent in areas of high HBV prevalence
- Secondary: gastroenterologists, infectious disease specialists, and other clinicians involved in the care of patients at risk for HBV

The target audience for the HCV curriculum includes:

- PCPs, OB/GYNs, NPs, PAs, hepatologists, gastroenterologists, infectious disease physicians, and others involved in the care of patients with hepatitis.

INTERNET CME POLICY

The Office of Continuing Medical Education (CME) at the Johns Hopkins University School of Medicine is committed to protecting the privacy of its members and customers. The Johns Hopkins University SOM maintains its Internet site as an information resource and service for physicians, other health professionals, and the public.

Continuing Medical Education at the Johns Hopkins University School of Medicine will keep your personal and credit information confidential when you participate in an Internet-based CME program. Your information will never be given to anyone outside of the Johns Hopkins University School of Medicine program. CME collects only the information necessary to provide you with the services that you request.

DISCLAIMER STATEMENT

The opinions and recommendations expressed by faculty and other experts whose input is included in this program are their own. This enduring material is produced for educational purposes only. Use of the Johns Hopkins University School of Medicine name implies review of educational format design and approach. Please review the complete prescribing information for specific drugs or combinations of drugs, including indications, contraindications, warnings, and adverse effects, before administering pharmacologic therapy to patients.

STATEMENT OF RESPONSIBILITY

The Johns Hopkins University School of Medicine takes responsibility for the content, quality, and scientific integrity of this CME activity.

STATEMENT OF NEED

Through discussions with experts in the specialty of HBV, a survey of participants from previous Johns Hopkins CME activities, and a review of current literature, the following core learning gaps have been identified:

HCV

- Clinicians do not adequately identify which of their patients are at highest risk for HCV infection or effectively interpret testing results.
- Clinicians need to understand best practices in how to identify and manage HCV treatment-related side effects.
- Clinicians need improved awareness of how newly emerging therapies impact therapeutic decision-making in HCV infected and HIV/HCV co-infected patients.
- Clinicians are unaware of new non-invasive techniques to stage liver disease.
- Clinicians need to understand best practices in identifying cirrhosis and HCC in patients infected with HCV.

HBV

- Clinicians do not effectively identify their patients at risk for HBV.
- Clinicians are unaware of new non-invasive techniques to stage liver disease.
- Clinicians need to understand best practices in identifying cirrhosis and HCC in patients infected with HBV.

PLANNER DISCLOSURES

As a provider accredited by the Accreditation Council for Continuing Medical Education (ACCME), it is the policy of the Johns Hopkins University School of Medicine Office of Continuing Medical (OCME) to require signed disclosure of the existence of financial relationships with industry from any individual in a position to control content of a CME activity sponsored by OCME. Members of the Planning Committee are required to disclose all relationships, regardless of their relevance to the activity content. Faculty are required to disclose only those relationships that are relevant to their specific presentations. The following relationships have been reported for this activity:

- **Mark S. Sulkowski, MD**, has disclosed that he has served as a consultant for AbbVie, Inc., Boehringer Ingelheim Pharmaceuticals, Inc., Bristol Myers-Squibb, Gilead, Janssen, Merck and Vertex Pharmaceuticals Incorporated. He has received grant/research funding from AbbVie, Inc., Boehringer Ingelheim Pharmaceuticals, Inc., Bristol Myers-Squibb, Gilead, Janssen, Merck and Vertex Pharmaceuticals Incorporated, and has served on a steering committee for Pfizer, Inc.
- **Raymond T. Chung, MD**, has disclosed that he has served as a consultant for AbbVie, Inc. and Idenix and has received grant/research funding from Gilead and Mass Biologics.

No other planners have indicated that they have any financial interests or relationships with a commercial entity.

CONFIDENTIALITY DISCLAIMER FOR CME CONFERENCE ATTENDEES

I certify that I am attending a Johns Hopkins University School of Medicine CME activity for accredited training and/or educational purposes.

I understand that while I am attending in this capacity, I may be exposed to "protected health information," as that term is defined and used in Hopkins policies and in the federal HIPAA privacy regulations (the "Privacy Regulations"). Protected health information is information about a person's health or treatment that identifies the person.

I pledge and agree to use and disclose any of this protected health information only for the training and/or educational purposes of my visit and to keep the information confidential.

I understand that I may direct to the Johns Hopkins Privacy Officer any questions I have about my obligations under this Confidentiality Pledge or under any of the Hopkins policies and procedures and applicable laws and regulations related to confidentiality. The contact information is: Johns Hopkins Privacy Officer, telephone: 410-735-6509, e-mail: HIPAA@jhmi.edu.

"The Office of Continuing Medical Education at the Johns Hopkins University School of Medicine, as provider of this activity, has relayed information with the CME attendees/participants and certifies that the visitor is attending for training, education and/or observation purposes only."

For CME Questions, please contact the CME Office at (410) 955-2959 or e-mail cmenet@jhmi.edu.

For CME Certificates, please call (410) 502-9634.

Johns Hopkins University School of Medicine
Office of Continuing Medical Education
Turner 20/720 Rutland Avenue
Baltimore, Maryland 21205-2195

Reviewed & Approved by:
General Counsel, Johns Hopkins Medicine (4/1/03)
Updated 4/09

HARDWARE & SOFTWARE REQUIREMENTS

PC: Internet Explorer (v6 or greater), or Firefox, MAC: Safari or Firefox

All rights reserved – The Johns Hopkins University School of Medicine.

MR. BOB BUSKER: Welcome to this *eViralHepatitis Review* Podcast.

eViralHepatitis Review is presented by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing. This program is supported by educational grants from AbbVie Inc., Boehringer Ingelheim Pharmaceuticals, Inc. and Genentech, Inc.

Today's program is a companion piece to our eViralHepatitis Review newsletter issue, *HCV Screening and Natural History*.

Our guest is that issue's author, Dr. David Thomas from the Johns Hopkins University School of Medicine.

This activity has been developed for primary care physicians, OB/GYNs, nurse practitioners, physician assistants, hepatologists, gastroenterologists, infectious disease physicians, and others involved in the care of patients infected or at risk for infection with hepatitis C.

There are no fees or prerequisites for this activity.

The Accreditation and Credit Designation Statements can be found at the end of this podcast. For additional information about accreditation, Hopkins policies and expiration dates, and to take the post-test to receive credit online, please go to our website newsletter archive, www.eviralhepatitisreview.org, and click on the Volume 3, Issue 10 podcast link.

Learning objectives for this audio program are, that after participating in this activity, the participant will demonstrate the ability to:

- Discuss why patients with no risk factor except being born between 1945 and 1965 should be tested for HCV.
- Describe current noninvasive testing that can be used to detect cirrhosis.
- Explain why HCV RNA should be used to detect acute HCV infection.

I'm Bob Busker, managing editor of eViralHepatitis Review. On the phone we have with us Dr. David Thomas, Professor of Medicine and Director of the Division of Infectious Diseases at the Johns Hopkins University School of Medicine in Baltimore.

Dr. Thomas has indicated that he has received grants and/or research support from Gilead Sciences, Inc. and Merck.

He has also indicated that his discussion today will not reference the unlabeled or unapproved uses of any drugs or products.

Dr. Thomas, welcome to this eViralHepatitis Review Podcast.

DR. THOMAS: It's a pleasure to participate.

MR. BUSKER: In your newsletter issue, Doctor, you reviewed the recent literature describing the rationale behind the CDC and USPTS recommendations for major changes in the screening of Americans for hepatitis C. What I'd like to do today is explore how some of that information can be translated into clinical practice. So start us off, if you would, with a patient description.

DR. THOMAS: Imagine a 57 year old man presenting to a general medicine practice with hypertension. He's coming in just for a routine checkup.

MR. BUSKER: So this is a simple routine checkup. Why should the physician even be thinking about hepatitis C in this patient?

DR. THOMAS: Now that's a good question because on the face of it there's nothing about hepatitis C, he's coming in for a routine blood pressure check and isn't endorsing any particular risk factors for hepatitis C. However, just because of when he was born and specifically having been born between 1945 and 1965, his risk of having hepatitis C is five-fold higher than if he were born in other years as an adult. And that puts him in a special group that merits at least one test for hepatitis C infection.

The other factor that enters into the decision to do a hepatitis C test is the fact that we have highly reliable tests available for detecting hepatitis C infection. The typical test is an antibody test to detect prior exposure to hepatitis C, and that can be done in nearly every commercially available lab in the United States. More recently, the FDA's approved point of care tests that can also be done right in a doctor's office in some instances to detect hepatitis C and to be able to provide the information after 20 minutes of waiting.

The final factor that comes into the recommendation to test this individual, not only does he have a five-fold increased risk of having it, not only do we have tests that can detect the infection, but also many individuals have hepatitis C infection and don't even know that they have it. You might wonder, well, shouldn't he already know, shouldn't there be some symptoms, shouldn't he be experiencing some sort of symptoms that make you think he has hepatitis C? The answer to that is no. About half of individuals that have hepatitis C infection aren't even aware of their status.

MR. BUSKER: Following up on what you just said, what are the symptoms that someone who is positive for HCV would likely show?

DR. THOMAS: The interesting issue with hepatitis C is the kind of symptoms that you have are difficult to pinpoint to the hepatitis C infection. For example, persons with hepatitis C compared to those without hepatitis C are more likely to experience fatigue and achy pains in their joints, but those symptoms are not specific enough to hepatitis C to be able to make most physicians think the patient must have hepatitis C infection, so I'll do a test. The classic sign of a problem with your liver is jaundice, and jaundice is rare in persons with hepatitis C; it only occurs after decades of infection, when the liver is already failing, and at that point, it's really often too late to treat anyway. So using symptoms to detect hepatitis C is really not reliable.

With my hepatitis C infected patients I'll often compare it to your car and using the amount of gas that you have in your car, as there is really no symptom of when your car is running out of gas until it's too late, until the car is out of gas and it won't run anymore. And hepatitis C is a lot like that, for most of the time that you have hepatitis C, there really aren't any specific symptoms that tell you that you have it, or even in many instances whether it's getting worse.

MR. BUSKER: All right, so this patient: he doesn't have any symptoms. What kind of risk factors might he have?

DR. THOMAS: This particular patient doesn't endorse any risk factors, other than having been born between 1945 and 1965. There are risk factors for hepatitis C infection, and persons with those risk factors have a much higher rate of hepatitis C infection than persons without them.

For example, anyone who had a blood transfusion before 1992 is at increased risk of hepatitis C infection, and that simply relates to the fact that hepatitis C testing of blood donations wasn't really highly effective until 1992. And so units that were received before then, and frankly any type of blood product that was received prior to effective screening tests would put an individual at increased risk.

Another hepatitis C risk factor is having ever used injection drugs. That's probably the strongest hepatitis C risk factor and one of the interesting parts of that is that even a little bit of injection drug use, for example, that someone might have done 20 or 30 years ago would put someone at increased risk.

Drug use became fashionable during the late 1960s and through the 1970s in the United States, and individuals who participated in brief periods of drug use during the '60s and '70s don't consider themselves drug users now. They wouldn't, for example, come into their physician 30 years later coming in for a blood pressure check and say "I was a drug user and I consider myself a drug user." That's just not the way they think about themselves. And often would be reluctant, even if they did remember having done that kind of thing, would be reluctant to bring it up with their primary care doctor who might also be someone that they play tennis with on the weekends, for example.

And so for a lot of those reasons, that's the risk factor that's least often endorsed and often missed in busy health care practices. There are also others, such as having unexplained elevated liver enzymes, and having been on hemodialysis and those sorts of things, even individuals that use cocaine intranasally are at increased risk of hepatitis C infection.

Collectively, those risk factors, if they're asked carefully in a nonjudgmental way, can identify even up to 80 percent of persons with hepatitis C. But in study after study that's been done in primary care practices, such as the study that we reviewed in the newsletter by Spralding and coworkers, most practices don't identify persons with those types of risk factors, and up to half of individuals in the United States with hepatitis C have not yet been identified.¹

MR. BUSKER: One key question we haven't addressed: how is this patient going to benefit from finding out whether or not he has hepatitis C?

DR. THOMAS: Part of the impetus for hepatitis C testing is the availability of treatments that can cure hepatitis C infection. There once was a time when we were very nihilistic about hepatitis C testing. In fact, when the test first came out in the early '90s, some authorities questioned whether it was advisable to test persons at all because the lack of proven treatments only led to the situation where a person would know they had hepatitis C infection and then feel depressed and really be worse off perhaps than they were before.

But there are several important benefits to testing that one should consider. First of all, when you find out that someone has hepatitis C, you can tell them to reduce the amount of alcohol that they ingest and that will reduce the likelihood that they'll develop cirrhosis or serious consequences from hepatitis C infection.

Number two, you can talk to them about trying not to infect other individuals and being particularly careful about not getting their blood on individuals, and having sex partners tested for hepatitis C and those sorts of things.

Number three, you can give them vaccinations for hepatitis A and B to prevent even further damage to their liver that could occur if they were to acquire another hepatitis infection.

And finally, you can consider the indication for treatment. And effective treatments for hepatitis C are available, and they are rapidly improving. And that's really one of the major forces behind the expanded interest in hepatitis C testing that we're currently seeing from the Centers for Disease Control. The availability of effective and safe treatments that can cure infection and prevent the long-term consequences is the main reason why this individual with asymptomatic hypertension should be tested for hepatitis C.

MR. BUSKER: Thank you for presenting that case and that discussion, Doctor Thomas. Let me ask you to describe another patient for us now.

DR. THOMAS: So consider a 34 year old woman with hepatitis C who has an ALT level of 22 and presents to your office. She's been reluctant to come to the office because she's afraid you're going to do a liver biopsy on her and she heard that those were particularly painful; she doesn't even like to have venipuncture. So the question would be how would you manage a patient like this?

MR. BUSKER: So this patient is from a different birth cohort and she is HCV positive. And, like most patients, she's afraid of a liver biopsy. Now we know a liver biopsy isn't required in all patients — but what kind of testing should all patients with hepatitis C receive?

DR. THOMAS: Everyone with hepatitis C antibodies needs at least an RNA test to make sure that they have ongoing infection. Antibodies to hepatitis C can either indicate ongoing hepatitis C infection or remote infection that occurred years or even decades earlier and was cleared. About 20 to 40 percent of individuals clear hepatitis C spontaneously. When they do so, the RNA is cleared from the blood but they continue to have antibodies just as after recovering from measles or mumps, or any other infectious disease.

Individuals that have hepatitis C antibodies and RNA also need to have a hepatitis C genotype test done, because that helps to decide what the best treatment would be and even gives us information about the likelihood of responding to treatment.

And finally, individuals with confirmed hepatitis C infection need to have a test done to figure out the stage of disease, how much scarring is there in the liver. And with a hepatitis C RNA test, a hepatitis C genotype and hepatitis C staging, most treatment decisions can be made.

MR. BUSKER: Let's focus on that last point for a second: what are the possible ways to stage the damage from hepatitis C?

DR. THOMAS: There are three approved methods for staging hepatitis C infection. The gold standard is liver biopsy. Liver biopsy was the first test that we had available for staging hepatitis C and remains the gold standard today. However, there are serious limitations to the liver biopsy.

First of all, the liver biopsy is expensive and painful and can have complications. About 1 out of 2,000 to 3,000 individuals who have a liver biopsy will end up with a serious complication requiring hospitalization. The liver biopsy also, even though it is the gold standard, can also give misleading information. And in particular, when the liver biopsy is too small, it can under stage the disease.

So there are also some other tests that have been approved for staging hepatitis C-related liver fibrosis. Some are blood tests, such as what's called the FibroSURE (called Fibro Test in Europe). Various laboratories use other blood tests to assess the stage of liver disease. These are combinations of individual test results that are put together using algorithms that estimate how much fibrosis is present in the liver.

In addition, there's a newly approved in April of 2013, the FibroScan test was approved. And that's an ultrasound-like test and that can be done even in a doctor's office to detect the amount of fibrosis. This test was actually the one that was used by Kirk and coworkers in the paper that we reviewed in the newsletter to assess the various determinants of hepatitis C-related fibrosis and evaluate the risks of HIV on liver fibrosis progression.²

So there are three tests that can be used to stage hepatitis C: the biopsy, FibroSURE or other blood tests, or the FibroScan.

MR. BUSKER: Because this information about how to determine staging is so important — and we know there are patients who avoid even considering treatment because of their fears of biopsy — let me ask you to briefly summarize the pros and cons of each of these staging options.

DR. THOMAS: The pros and cons of the liver biopsy. The pro is obvious, it's the gold standard, and what you see is what you get. If there's cirrhosis present on the biopsy, it's definitely there, there's no question about it. The cons are the pain, the expense, and the potential for complications.

The FibroScan, a noninvasive ultrasound-like test, is very good at detecting cirrhosis, but about 20 percent of the time no result is possible because of technical limitations with the scan itself.

The FibroSURE blood test is simple to perform and safe, but is sometimes inaccurate and misclassifies persons or fails to provide a convincing classification, especially when results of intermediate range are obtained.

MR. BUSKER: Let's apply that specifically to the patient you described — this 34 year old HCV positive woman with an ALT of 22. What would you do to stage her?

DR. THOMAS: In this woman I would first order a FibroSURE blood test and a FibroScan noninvasive test. First of all, I'd do that because I have a low pretest probability that she's going to have cirrhosis. It's a woman, she's young, and in most instances she wouldn't have had this infection very long, and probably with a low ALT level will not have cirrhosis or severe fibrosis. And so with these two noninvasive tests, I can often in a young woman convince myself that there is a low disease stage, and coupled with a very low pretest probability I can feel very secure managing her.

MR. BUSKER: Thank you, Doctor. And we'll return, with Dr. David Thomas from the Johns Hopkins University School of Medicine, in just a moment.

MS. JULIE MCARTHUR: Hello. I'm Julie McArthur, Adult Nurse Practitioner in the Division of Infectious Diseases at Johns Hopkins University. I'm one of the program directors of *eViralHepatitis Review*.

eViralHepatitis Review is a combination newsletter and podcast program delivered via e-mail to subscribers. Newsletters are published every other month. Each issue reviews the current literature in areas of importance to hepatologists, infectious disease specialists, primary care physicians, nurses, nurse practitioners and other clinicians caring for patients with viral hepatitis

Bi-monthly podcasts are also available as downloadable transcripts, providing case-based scenarios to help bring that new clinical information into practice in the exam room and at the bedside.

Subscription to *eViralHepatitis Review* is provided without charge or prerequisite.

Continuing education credit for each issue and each podcast is provided by The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing. For more information on this educational activity, to subscribe to and receive *eViralHepatitis Review* without charge, and to access back issues, please go to our website: www.eviralhepatitisreview.org

MR. BUSKER: Welcome back to this *eViralHepatitis Review* podcast. I'm Bob Busker, managing editor of the program. Our guest is Dr. David Thomas, Director of the Division of Infectious Diseases at the Johns

Hopkins University School of Medicine. And our topic is *HCV Screening and Natural History*.

We've been discussing how some of the new information Dr. Thomas reviewed in his newsletter issue can be applied in clinical practice. So if you would, Doctor, please us present with another patient.

DR. THOMAS: Consider the circumstance of a 24 year old who has a needle stick in a hospital from a patient with hepatitis C, but not HIV. So the patient is hepatitis C positive and let's say this is a 25 year old intern in his first year in the hospital who is exposed by needle stick.

MR. BUSKER: What immediate action should be taken in this kind of situation?

DR. THOMAS: Well the first thing that should occur is that there is some standard precautions in terms of general hygiene that the individual should implement. For example, washing the wound and obviously covering it if there is still any bleeding.

Secondly, the individual should report his needle stick quickly. All hospitals are required to have some capacity to handle needle stick exposure and to manage them. And so calling the needle stick hotline is the next step in this case.

The individual on the other end of the hotline, in this case the managing physician, is going to want to talk to the needle stick recipient and understand the nature of the needle stick, in particular, wanting to assess how large the inoculum could have been. That has to do with the size of the needle, the depth of the penetration, and of course, the status of the donor.

In this case, the intern, from his awareness of the patient, knows that the patient is hepatitis C RNA positive and HIV negative. The intern would also be asked was the patient hepatitis B positive and have you had hepatitis B vaccination and proven seroconversion to the hepatitis B vaccine.

I'll also point out that in this complex situation, some individuals use a genetic test. They test the DNA of the needle stick recipient for something called IL28B genotype. This refers to the DNA sequences around the genes for lambda interferon-3, which is also called IL28B. And it turns out that individuals with the

favorable genotype — often called CC, referring to being homozygous for a C allele at a particular position, 3,000 kilobases upstream from the lambda-3-interferon gene — are more likely to spontaneously resolve hepatitis C, so they're more likely to recover all by themselves. And some individuals would wait longer in an individual that is IL28BCC and give them the opportunity to spontaneously resolve while suggesting treatment sooner for an individual with the unfavorable T allele.

MR. BUSKER: The situation you presented was about an intern in a hospital. Is there any difference if this needle stick were to have happened in a PCP's office?

DR. THOMAS: No, the management of a needle stick exposure is the same no matter where it occurs, and actually it doesn't even have to be a needle stick. What we're talking about in this case is the general issue of post-exposure management of hepatitis C to the situation where an exposure has occurred to a hepatitis C-positive blood source.

MR. BUSKER: So this individual who received a needle stick — or had, as you said, exposure to a hepatitis C-positive blood source — what can you tell us about his actual risk of getting hepatitis C infection?

DR. THOMAS: The risk of hepatitis C infection after a needle stick is approximately 1 to 4 percent, and that risk depends on the size of the inoculum. And to some extent the inoculum size is determined by the amount of virus in the donor. An individual with a very high viral load, for example, let's say 7 logs iU/mL is more likely to transmit than an individual with a low hepatitis C viral load, and especially an individual who's cleared hepatitis C infection either from treatment or naturally. To drive that point home, if an individual is exposed to a person without hepatitis C RNA in their blood, the risk would be essentially nil.

Now the inoculum size is also determined by how much blood went from the donor into the recipient, and oftentimes the best assessment of that is the kind of needle that the individual was exposed to. The risk is lowest with a solid-bore needle because there is really no opportunity for large amounts of blood to pool in a solid bore needle, like such as the ones that are used for suturing.

In contrast, a hollow bore needle, especially one of a large gauge, let's say an 18 gauge needle, can harbor a significant amount of blood in the bevel of the needle, and that blood can be inoculated into the recipient at the time of the needle stick.

The third issue that determines the likelihood of transmission is the depth of penetration and the risk is, of course, lowest if there is simply a scratch on the surface of the skin, and highest if there's deep penetration into subcutaneous tissues.

MR. BUSKER: This 24/25 year old intern who received this needle stick — how would you monitor him to see if infection does occur?

DR. THOMAS: After a hepatitis C exposure and after appropriate counseling, and after appropriate initial hygiene, the next step is to make sure that baseline testing has been complete. And to be specific, an individual at the time of the exposure should have antibody tests for hepatitis C to make sure that they were not already infected. They should also follow up with hepatitis C testing.

Now the hepatitis C testing after an exposure is variable. I recommend testing for hepatitis C RNA at two and four weeks after an exposure and then hepatitis C antibody test six months later. The reason for my recommendation is that hepatitis C RNA is often detected very early, as early as 10 days after an exposure, and I like to know when there's infection early on so that I can monitor the course of the infection to see if there is evidence of spontaneous resolution.

The antibody test at 6 months is the catchall, it's the test that I do to make sure that I didn't miss any infection, but is often not informative. So after hepatitis C exposure, I recommend RNA testing at two and four weeks, and hepatitis C antibody testing six months after the exposure.

MR. BUSKER: : If any of these tests turn up positive, what action should be taken?

DR. THOMAS: The reason we do hepatitis C testing early on is to provide information to the exposed health care worker about whether or not they've been infected. One of the important early messages if a person is infected is to be careful not to infect other household contacts. I try to remember to always

counsel the recipient to start using condoms and to avoid sexual transmission of hepatitis C.

Now individuals hearing this advice might recognize that it differs from the advice we give to persons with chronic hepatitis C in whom we do not routinely recommend the use of condoms. But after acute hepatitis C, there's reason to believe that an individual would be more infectious, the viremia is at least a log higher in the blood and there are no antibodies yet in the blood to complex the virus and reduce its infectivity. So I take the safest measure and recommend the use of a condom and safe sex, even with a stable partner after a needle stick-acquired hepatitis C infection.

In addition, we detect hepatitis C infection as early as possible because there's evidence that hepatitis C can be treated easier when treatment is initiated in the first 8 to 12 weeks after infection occurs. These data are all accumulated with interferon-based treatments and interestingly apply to both the use of standard interferon, the very first interferons that we used, as well as the pegylated interferon and the combined use of pegylated interferon and ribavirin. Very brief courses of 12 to 24 weeks of all of these combinations have been shown to be highly effective in acute hepatitis C infection and more effective than when given after a year of infection.

So because of those observations, we've tried to emphasize the importance of detecting hepatitis C in the acute phase, both to prevent transmission to other individuals and to optimize the chance of curing the particular needle-stick recipient.

I will say that this dynamic is changing. As we come up with improvements in our treatment of chronic hepatitis C, the decrement in the likelihood of responding compared to the acute and chronic phase is diminishing. And some are now wondering if we should even wait in all individuals, give them the opportunity to spontaneously resolve and allow the others to transition to the chronic phase, given the high likelihood of being able to cure them with safe medications. So that's a change in the treatment paradigm that is being introduced by the rapid development of safer, more effective treatments for chronic hepatitis C.

MR. BUSKER: You talked about the pros of early treatment. What are the cons? Is there a downside to early treatment?

DR. THOMAS: Well since treatment of acute hepatitis C is currently based on interferon and ribavirin, the cons of treatment have to do with the side effects of those medications. In individuals that are, let's say this intern who's up all night and busy taking care of patients, it can be difficult to withstand an interferon and ribavirin course. And so the principal con is that treatment side effects would be experienced that might not be necessary if one were to wait for spontaneous resolution or wait several years for interferon-sparing treatment.

MR. BUSKER: Doctor Thomas, thank you for today's cases and discussion. I'd like to ask you to give us a summary, if you would, about how some of the things we've talked about today are changing the approach to hepatitis C management.

DR. THOMAS: So the rapid development of new hepatitis C treatments is one of the most exciting things that's going on right now in medicine. It affects many of the approaches that we have to hepatitis C, beginning with increasing the enthusiasm for hepatitis C testing. As I mentioned before, one of the major impetuses for testing more people for hepatitis C is the knowledge that once we find them to be infected, we can cure them more safely with new hepatitis C treatments.

In addition, even with this issue of acute hepatitis C infection, the availability of safe oral medications has started to transform our approach, and some individuals are even withholding treatment from individuals with acute infection unless there's an urgent reason to treat them.

MR. BUSKER: Thank you for sharing your thoughts, Doctor. To wrap things up, let review today's discussion in light of our learning objectives. So to begin: why patients with no risk factor except being born between 1945 and 1965 should be tested for HCV.

DR. THOMAS: So the main reason for individuals born between 1945 and 1965 being tested for hepatitis C include a five-fold increased risk of infection, that often their infection is unrecognized, and the infection

can be cured, and in doing so, prevent the risk of hepatocellular carcinoma and end stage liver disease.

MR. BUSKER: And the current noninvasive testing that can be used to detect cirrhosis.

DR. THOMAS: There are three tests that can be used to detect cirrhosis. One is the liver biopsy, which is invasive, and there are two noninvasive tests that are approved, the FibroSURE and the FibroScan.

MR. BUSKER: And finally: why HCV RNA testing should be used to detect acute HCV infection.

DR. THOMAS: After acute hepatitis C infection, HCV RNA can be detected for up to a month before hepatitis C antibodies. Therefore, in situations in which it is important to diagnose hepatitis C in the acute phase, the RNA test is preferred.

MR. BUSKER: Dr. David Thomas from the Johns Hopkins University School of Medicine, thank you for participating in this eViralHepatitis Review Podcast.

DR. THOMAS: It's been a pleasure.

MR. BUSKER: This podcast is presented in conjunction with the eViralHepatitis Review Newsletter, a peer-reviewed literature review certified for CME/CE credit, emailed monthly to clinicians treating patients with viral hepatitis.

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education, through the joint sponsorship of the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing. The Johns Hopkins University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

The Johns Hopkins University School of Medicine designates this enduring material for a maximum of 0.5 *AMA PRA Category 1 Credits*[™]. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The Institute for Johns Hopkins Nursing is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

For nurses, this 0.5 contact hour Educational Activity is provided by The Institute for Johns Hopkins Nursing. Each podcast carries a maximum of 0.5 contact hour.

This educational resource is provided without charge, but registration is required. To register to receive eViralHepatitis Review via e-mail, please go to our website, www.eViralHepatitisReview.org.

The opinions and recommendations expressed by faculty and other experts whose input is included in this program are their own. This enduring material is produced for educational purposes only.

Use of names of the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing implies review of educational format, design, and approach. Please review the complete prescribing information for specific drugs, combinations of drugs, or use of medical equipment — including indication, contraindications, warnings, and adverse effects — before administering therapy to patients.

Thank you for listening.

eViralHepatitis Review is supported by educational grants from AbbVie, Inc., Boehringer Ingelheim Pharmaceuticals, Inc., and Genentech, Inc.

This program is copyright with all rights reserved, by The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing.

REFERENCE

1. Spradling PR, Rupp L, Moorman AC, et al; Chronic Hepatitis Cohort Study Investigators. Hepatitis B and C virus infection among 1.2 million persons with access to care: factors associated with testing and infection prevalence. *Clin Infect Dis.* 2012 Oct;55(8):1047-1055.
2. Kirk GD, Mehta SH, Astemborski J, et al. HIV, age, and the severity of hepatitis C virus-related liver disease: a cohort study. *Ann Intern Med.* 2013 May 7;158(9):658-666.